

## **Section II (Remarks)**

### **Amendment of Claims 46, 47 and 49**

Claim 46 has been amended herein to further specify the invention. Amended claim 46 now recites a nanoparticulate membrane “wherein an oxidoreductase enzyme and polymeric redox mediator capable of transferring electrons are diffusibly dispersed in said nanoparticulate membrane to allow diffusion thereof within the membrane and into a test sample, when the membrane is exposed to a said test sample.”

Such amendment therefore elaborates the meaning of the term “diffusibly dispersed” and specifies that the diffusional mobility of the oxidoreductase enzyme and polymeric redox mediator encompass diffusion within the membrane as well as into a test sample comprising the analyte when the membrane is exposed to the sample.

The amended language of claim 46 is fully consistent and supported by the originally filed disclosure of the application. See, for example, paragraph [0053] (“[t]he sample chamber 14, with the nanocomposite membrane 18 therein, receives the analyte for analysis thereof by wicking or capillary action ...the diffusible redox mediator may diffuse rapidly into the analyte”), paragraph [0065] (“[m]ediators, enzymes and analytes such as glucose can then move freely within this layer, whereas interfering species, such as red blood cells containing oxygenated hemoglobin are excluded from entering the membrane due to electrostatic repulsion”), paragraph [0073] (“diffusional mediators are typically lower in molecular weight and can leach out of the electrode...in the sample”) and paragraph [0136] (“glucose and mediators move freely within this layer”).

Claim 47 has been amended to correct the capitalization of the word “Claim,” for consistency with the other claims now pending in the application.

Claim 49 has been amended for consistency with claim 46, from which it depends, and the capitalization of the word “Claim” has been corrected for consistency with other claims in the application.

### **Rejection of Claims 46-56 Under 35 USC 103 (A) Over Rauh in view of Bu**

In the January 9, 2009 Office Action, claims 46-56 were rejected under 35 USC 103(a) as unpatentable over Rauh in view of Bu. This rejection is traversed in application to the claims as now amended herein. Reconsideration of the patentability of the amended claims is requested, in light of the following remarks.

### **Patentability of Claims 46-56 Over the Art**

In the statement of rejection of page 3 of the January 9, 2009 Office Action, it is stated that “[t]he claims differ from Rauh in that they specify the matrix is an acrylamide polymer.” In fact, the claims now pending in the application do not specify any matrix nor do they refer to an acrylamide polymer matrix.

Claim 46, from which all other pending claims directly or indirectly depend, recites a nanoparticulate membrane “wherein an oxidoreductase enzyme and polymeric redox mediator capable of transferring electrons are diffusibly dispersed in said nanoparticulate membrane to allow diffusion thereof within the membrane and into a test sample, when the membrane is exposed to a said test sample.” The combination of Rauh in view of Bu fails to disclose or provide any derivative basis for such a nanoparticulate membrane.

At page 4 of the January 9, 2009 Office Action, concerning Rauh, it is contended “that the membrane of Rauh teaches substances including the same enzymes and mediators as presently claimed are diffusibly dispersed within the membrane.” This statement then is followed by references to immobilization teachings in Rauh (“co-immobilization of bio-molecules in the membrane is described...various methods of immobilizing the enzyme in the membrane are discussed” (Office Action, p. 4, lines 11-13), after which it is concluded that “[i]t would seem

that this description of the dispersion of the enzyme of the matrix would be encompassed by diffusibly dispersed.”

In fact, the foregoing statements in the Office Action ignore the import of the word “diffusibly” as specifying the dispersed character of the oxidoreductase enzyme polymeric redox mediator in the membrane of applicants’ claimed invention.

Because the oxidoreductase enzyme and polymeric redox mediator in the membrane of applicants’ claimed invention are diffusibly dispersed in the membrane and thus capable of diffusion, such species are mobile and not immobilized as taught by Rauh. This basis of distinction has been further specified in amended claim 46 by the recital by the oxidoreductase enzyme and polymeric redox mediator as being “diffusibly dispersed in said nanoparticulate membrane to allow diffusion thereof within the membrane and into a test sample, when the membrane is exposed to a said test sample.”

In this respect, the Rauh teachings are clear that oxidoreductase is immobilized in the membrane, so that after preparation of the membrane the position of the oxidoreductase is fixed and unchanging. See, for example, Rauh at:

- column 3, lines 56-64 (“a sensor electrode that responds to molecular species recognized by the immobilized biomolecules...a matrix incorporating redox centers which can transfer an electron directly to/from an active redox center within the immobilized biomolecule”);
- column 4, line 66 (“Co-immobilization of biomolecules”);
- column 6, lines 19-22 (“Enzyme solutions may also be dropped onto individual array elements and allowed to become immobilized by absorption, similar to well known enzyme immobilizations in porous silica and titania”);
- column 6, lines 37-38 (“enzyme entrapment in a hydrous Ir oxide matrix”);
- column 8, lines 66-67 (“Additional electron transfer mediators can be co-immobilized into the oxide matrix”);
- column 9, lines 57-58 (“the hydrous oxides can be used to immobilize any biomolecule in the hydrous metal oxide”);

- column 10, lines 9-10 (“Immobilizing enzyme substrates in the hydrous metal oxide matrix”);
- column 11, lines 1 (“entrap GOx, e.g., polypyrrole”) and lines 33-34 (“some of the GOx is buried deeper in the Ir oxide matrix and is more protected”); and
- column 12, lines 34-35 (“the enzyme GOx becomes trapped in the oxide matrix”),

as teaching that the enzyme is immobilized in the membrane of Rauh.

See also **Appendix A** of this Response, containing a copy of the title page, copyright page, and page containing the definition of “immobilized,” from Webster’s Encyclopedic Unabridged Dictionary of the English Language (Portland House, 1996), wherein “immobilized” is defined as “to make immobile; fix so as to be or become immovable.”

It is clear from the foregoing that the enzyme in the Rauh membrane is not in any way “diffusibly dispersed,” as required by applicants’ amended claims. Contrariwise, the enzyme in the Rauh membrane is immobilized, and cannot diffuse within and out of the membrane, as required by the presently claimed invention. In applicants’ claimed invention, “an oxidoreductase enzyme and polymeric redox mediator capable of transferring electrons are diffusibly dispersed in said nanoparticulate membrane to allow diffusion thereof within the membrane and into a test sample, when the membrane is exposed to a said test sample” (claim 46, as herein amended).

Bu has been cited for showing acrylamide polymer with polyvinylferrocene for sensor membranes and function of the material. Such showing, however, does not alter the fact that Rauh teaches a membrane containing an immobilized enzyme, contrary to the requirements of applicants’ claimed invention. As pointed out in applicants’ last Response filed November 20, 2008, Bu at page 3953 teaches “fixed redox-active VF residues,” i.e., a redox polymer that is present in a fixed position and that is not “diffusibly dispersed ... to allow diffusion thereof within the membrane and into a test sample” as required by applicants’ claimed invention.

The combination of Rauh in view of Bu therefore does not provide disclosure of, or any logical basis for, a membrane wherein “an oxidoreductase enzyme and polymeric redox mediator capable of transferring electrons are diffusibly dispersed in said nanoparticulate membrane to

allow diffusion thereof within the membrane and into a test sample, when the membrane is exposed to a said test sample,” as required by presently amended claim 46, from which all remaining claims 47-56 directly or indirectly depend.

At page 4 of the Office Action, it is stated that “for the membrane to function, the analyte must have contact with both the enzyme and the mediator and for the reactions to continue beyond initial contact, the enzyme and mediator must be maintained in such a fashion that the contacting continues for the desired time period.” In this respect, it is noted that applicants’ membrane allowing the enzyme and polymeric redox mediator to diffuse freely, functions extremely effectively as demonstrated by the results of Examples 5-8 at pages 36-46 of the present application.

For all the foregoing reasons, it is requested that the rejection of claims 46-56 based on Rauh in view of Bu be withdrawn.

### **CONCLUSION**

Claims 46-56 have been shown to be patentably differentiated over Rauh in view Bu, and such claims are now in form and condition of allowance.

Issue of a Notice of Allowance therefore is requested.

Respectfully submitted,

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# **APPENDIX A**

# **Webster's Encyclopedic Unabridged Dictionary of the English Language**

PORTLAND HOUSE



#### ACKNOWLEDGMENTS AND PERMISSIONS

The "A dictionary of the English Language" section of this (*Webster's Encyclopedic Unabridged Dictionary*) is based on the first edition of *The Random House Dictionary of the English Language, the Unabridged Edition*, copyright © 1983.

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